

Krauss et al.
Application No.: 09/844,061
Page 5

PATENT

Remarks

Amendments

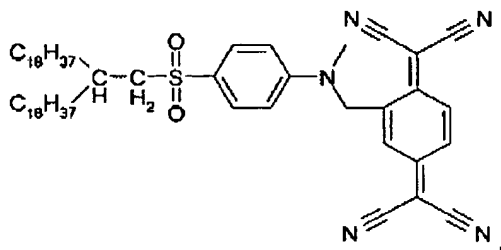
The amendment of claim 1 above (a) corrects the structure (to place the R superscripts correctly), and (b) corrects a typographical error. No new matter is added thereby.

Rejection Under §102

A. *Sato et al.*

Claims 1-19 and 38-43¹ were rejected as anticipated under §102(b) over Sato et al., US 4,987,023. Applicants respectfully traverse.

The compound disclosed in Sato to which the Examiner refers,



is not within Applicants' claims. Note that in claim 1, R² may be alkyl. However, "alkyl" is defined in the specification as "a linear saturated monovalent hydrocarbon radical of one to six carbon atoms or a branched saturated monovalent hydrocarbon radical of three to six carbon atoms..." (Specification at p. 3, lines 17-18). The C₃₈ moiety in Sato's compound contains far more than six carbon atoms, and thus cannot anticipate the current claims.

B. *Berman et al.*

Claims 1-19 and 28-43² were rejected as anticipated under §102(b) over Berman et al., US 4,857,530. Applicants respectfully traverse.

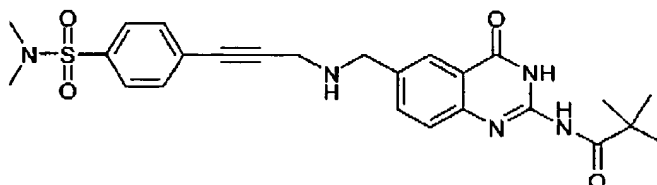
The compound cited by the Examiner at Col. 7, lines 65-70 has the following structure:

¹ Note: the Office action states that claims 1-19 and 28-43 are rejected; however, as claims 20-37 have been canceled, Applicants assume that rejection of claims 1-19 and 38-43 was intended.

² See footnote 1.

Krauss et al.
Application No.: 09/844,061
Page 6

PATENT

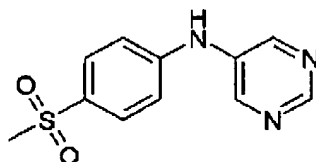


Applicants respectfully point out that this compound does not fall within claim 1, because it lacks an N bound to the phenyl ring (Berman's compound has a propynyl group between the nitrogen and the phenyl ring). Further, note that propynyl does not fall within the definition of biradical A, as $-(CR_2)_n-$ where R is H or alkyl does not result in any unsaturation. Additionally, note that while B may be heteroaryl, "heteroaryl" is limited in claim 1 to furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl, and pyridazinyl: it does not include quinazolinyl. Thus, Applicants submit that Berman fails to anticipate the present claims.

C. *Okada et al.*

Claims 1-19 and 28-43³ were rejected as anticipated under §102(b) over Okada et al., US 5,538,976. Applicants respectfully traverse.

Okada disclosed the compound 5-(4-methansulfonylphenylamino)pyrimidine:



at column 14, line 25, as cited by the Examiner. However, this compound does not fall within the scope of claim 1. Note that claim 1 requires an alkylene bridge ("A") of at least one carbon atom between the amine and the heteroaryl group B, which is absent in the Okada compound. Further, the heteroaryl groups used in the present invention for group B are limited in claim 1 to furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl, and pyridazinyl: pyrimidinyl is not included. Thus, Okada fails to anticipate the claimed invention.

³ See footnote 1.

Krauss et al.
Application No.: 09/844,061
Page 7

PATENT

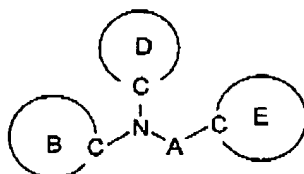
Rejection Under §103

Claims 1-19 and 38-43 were rejected as obvious under §103(a) over Sato, Berman, and Okada. Applicants respectfully traverse.

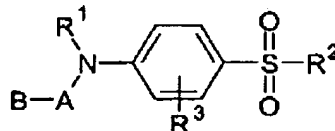
Sato disclosed organic compounds useful in the preparation of electronic components such as "display devices, rectifiers, switching devices, or light memory devices" (Sato at col. 2, lines 34-36.) As discussed above, the compounds disclosed by Sato are characterized by very large alkyl groups (C₃₈), and are outside the scope of Applicants' claims. Since Sato is drawn from a non-analogous art, it fails to provide any teaching or suggestion in combination with Berman or Okada.

Berman disclosed quinazoline derivatives asserted to be useful as thymidine synthase inhibitors for the treatment of cancer. As discussed above, compounds of the present invention do not include quinazolines. Berman fails to provide any suggestion or teaching to replace the quinazoline ring with a heterocycle within the scope of Applicants' claimed invention.

Okada disclosed aromatase inhibitors of the formula



where A is a bond, lower alkylene, etc., ring B is pyrimidine, pyridazine, or triazine, and rings D and E are each independently optionally substituted aryl or 5- or 6-membered heterocyclic groups. In contrast, the compounds claimed herein are COX I and COX II inhibitors (see, e.g., specification at page 33, lines 12-14) of the formula



To map the Okada compounds onto Applicants' claim 1, Okada's ring "E" (E_O) must correspond to Applicants' substituent B (B_A), because Applicants' "A" must contain at least one carbon atom, and Okada's rings B_O and D_O are connected directly to the central amine, without an alkylene linkage. Thus, the Okada rings B_O and D_O must be shown to correspond to Applicants' R¹ and the optionally

Krauss et al.
Application No.: 09/844,061
Page 8

PATENT

substituted $R^2SO_2C_6H_4-$ moiety. B_O is limited to pyrimidine, pyridazine, and triazine (Okada at col. 2, lines 8-9), and thus cannot be the $R^2SO_2C_6H_4-$ moiety. However, B_O cannot be R^1 either: R^1 is "alkyl, alkenyl, cyanoalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, heteroalkyl or alkylcarbonylalkyl" (see claim 1), which does not include pyrimidine, pyridazine, or triazine. Note that "heterocyclyl" is defined as non-aromatic (specification at p. 6, lines 14-15), and that "heteroaralkyl" requires an alkylene link (specification at p. 6, lines 9-11). Thus, Okada fails to teach or suggest the claimed compounds.

Further, the combination of Sato, Berman, and Okada fails to suggest or teach the claimed compounds. Sato is from a non-analogous art, and thus would not even be considered by one of ordinary skill in the art of medicinal chemistry.

To establish a prima facie case of obviousness under §103(a), the Office must point to statements in the art that would suggest or teach the claimed invention to one of ordinary skill in the art. Applicants fail to see any such teaching in the cited references. Sato teaches compounds useful for the fabrication of electronic components: the desired properties of these compounds are based on their dipole moments and charge transfer characteristics, not on their ability to bind to a target receptor or enzyme (or their ability to be formulated: the undersigned notes that the enormous C_{38} substituent would likely render the Sato compounds completely insoluble in water, and thus very difficult to administer effectively as a drug). Berman teaches quinazolines that inhibit thymidine synthase, while Okada teaches triaryl amines that inhibit aromatase. Applicants can discern no teaching in the cited art that would lead one of ordinary skill to pick and choose substituents from Sato, Berman, and/or Okada in such a way that one would arrive at the compounds claimed herein, particularly as none of the cited art compounds are COX I or COX II inhibitors. One of ordinary skill in the art would not expect that modifying a thymidine synthase inhibitor based on the structure of an aromatase inhibitor (or vice versa) would result in any advantageous properties at all, much less a compound having an unrelated activity.

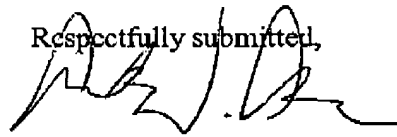
Thus, Applicants submit that no prima facie case of obviousness has been established, or can be established based on the cited references, and that the rejection is thus overcome.

Krauss et al.
Application No.: 09/844,061
Page 9

PATENT

Applicants respectfully submit that the application is now in condition for examination. Any questions regarding the application may be directed to the undersigned at the telephone or email addresses given below.

Respectfully submitted,



Grant D. Green
Reg. No. 31,259

March 9, 2005

Roche Palo Alto LLC
Patent Law Dept. M/S A2-250
3431 Hillview Avenue
Palo Alto, CA 94304
grant.green@roche.com
Direct Phone: 650-855-5311